

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

1.-4. (Canceled).

15. ~~(Previously presented)~~ *Actinosynnema pretiosum* strain PF4-4 having ATCC accession number PTA-3921.

16. ~~(Currently amended)~~ An enhanced *Actinosynnema pretiosum* strain that produces an ansamitocin in an amount of between about 1.2-fold and about 10-fold more than the amount produced by *Actinosynnema pretiosum* strain N-1231 (ATCC accession number 31565), said enhanced *Actinosynnema pretiosum* strain produced by a method comprising:

(a) treating a bacterial culture of *Actinosynnema pretiosum* with a mutagen,

(b) growing the treated bacterial culture of (a) under selective pressure,

(c) selecting an isolate from the product of (b) that exhibits increased production of an ansamitocin compared with the culture used in (a), and

(d) optionally repeating (a), (b) and (c) until an isolate that produces between about 1.2-fold and about 10-fold more of an ansamitocin than *Actinosynnema pretiosum* strain N-1231 is obtained.

3 7. ~~(Previously presented)~~ The enhanced *Actinosynnema pretiosum* strain according to claim 6, wherein the enhanced strain produces an ansamitocin in an amount of between 1.2-fold and 10-fold more than the amount produced by *Actinosynnema pretiosum* strain N-1231 (ATCC accession number 31565).

4. ~~(Previously presented)~~ The enhanced *Actinosynnema pretiosum* strain according to claim 2, wherein the enhanced strain produces an ansamitocin in an amount of between 1.8-fold and 10-fold more than the amount produced by *Actinosynnema pretiosum* strain N-1231 (ATCC accession number 31565).

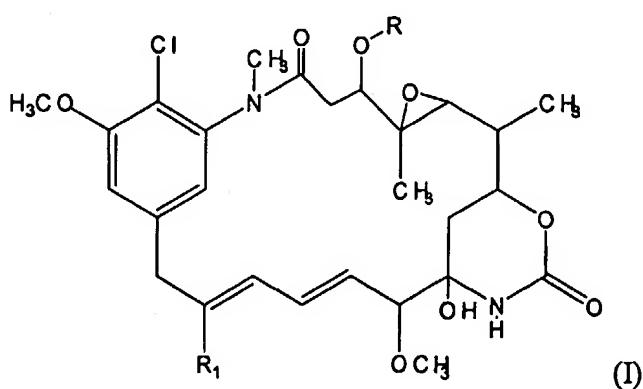
5. ~~(Previously presented)~~ The enhanced *Actinosynnema pretiosum* strain according to claim 2, wherein the enhanced strain produces an ansamitocin in an amount of between 5-fold and 10-fold more than the amount produced by *Actinosynnema pretiosum* strain N-1231 (ATCC accession number 31565).

10. (Canceled).

6. ~~(Previously presented)~~ The enhanced *Actinosynnema pretiosum* strain according to claim 6, wherein the ansamitocin is ansamitocin P-3.

7. ~~(Withdrawn)~~ A method for producing an ansamitocin, which comprises cultivating the enhanced *Actinosynnema pretiosum* strain of claim 6 in a culture medium comprising a suitable carbon source.

8. ~~(Withdrawn)~~ The method of claim 12, wherein said ansamitocin is one or more ansamitocins of formula (I) or isomers thereof:



wherein R is selected from the group consisting of hydrogen, acetyl, propionyl, isobutyryl, butyryl, and isovaleryl, and R₁ is selected from the group consisting of methyl and hydroxymethyl.

14. ~~(Withdrawn)~~ The method of claim 13, wherein R is isobutyryl and R₁ is methyl.

15. ~~(Withdrawn)~~ The method of claim 12, wherein said ansamitocin is ansamitocin P-3 and said carbon source comprises one or more carbon sources selected from the group consisting of valine, isobutyric acid, isobutyl alcohol, and isobutylaldehyde.

16. (Currently amended) An enhanced *Actinosynnema* strain that produces an ansamitocin in an amount of between about 1.2-fold and about 10-fold more than the amount produced by *Actinosynnema pretiosum* strain N-1231 (ATCC accession number 31565), said enhanced *Actinosynnema* strain produced by a method comprising:

(a) treating a bacterial culture of an *Actinosynnema* strain with a mutagen,

(b) growing the treated bacterial culture of (a) under selective pressure,

(c) selecting an isolate from the product of (b) that exhibits increased production of an ansamitocin compared with *Actinosynnema pretiosum* strain N-1231, and

(d) optionally repeating (a), (b) and (c) until an isolate that produces between about 1.2-fold and about 10-fold more of an ansamitocin than *Actinosynnema pretiosum* strain N-1231 is obtained.

17. (Previously presented) The enhanced *Actinosynnema* strain according to claim 16, wherein the enhanced strain produces an ansamitocin in an amount of between 1.2-fold and 10-fold more than the amount produced by *Actinosynnema pretiosum* strain N-1231 (ATCC accession number 31565).

wherein R is selected from the group consisting of hydrogen, acetyl, propionyl, isobutyryl, butyryl, and isovaleryl, and R₁ is selected from the group consisting of methyl and hydroxymethyl.

23. (Withdrawn) The method of claim 22, wherein R is isobutyryl and R₁ is methyl.

24. (Withdrawn) The method of claim 21, wherein said ansamitocin is ansamitocin P-3 and said carbon source comprises one or more carbon sources selected from the group consisting of valine, isobutyric acid, isobutyl alcohol, and isobutylaldehyde.

25.-33. (Canceled).

34. (Currently amended) A method of producing an enhanced *Actinosynnema* strain that produces an ansamitocin in an amount of between about 1.2-fold and about 10-fold more than the amount produced by a parental *Actinosynnema* strain from which the enhanced strain is derived, said method comprising:

- (a) treating a bacterial culture of an *Actinosynnema* strain with a mutagen,
- (b) growing the treated bacteria of (a) under selective pressure,
- (c) selecting for an isolate from of the product of (b) that exhibits increased production of an ansamitocin compared with the culture used in (a), and
- (d) optionally repeating (a), (b) and (c) until an isolate that produces between about 1.2-fold and about 10-fold more of an ansamitocin than the culture used in (a) is obtained.

35. (Canceled).

36. (Previously presented) The method of claim 34, wherein said *Actinosynnema* strain is a strain of an *Actinosynnema pretiosum*.

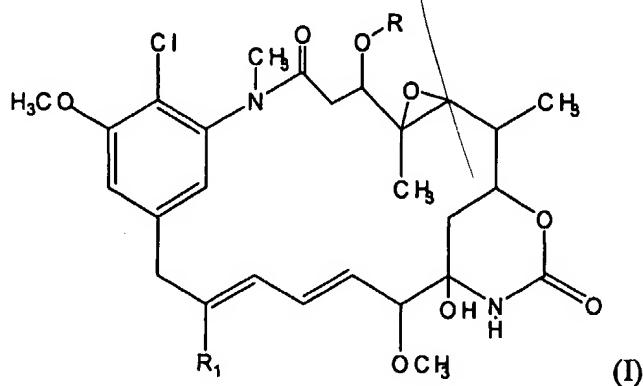
18. (Previously presented) The enhanced *Actinosynnema* strain according to claim 16, wherein the enhanced strain produces an ansamitocin in an amount of between 1.8-fold and 10-fold more than the amount produced by *Actinosynnema pretiosum* strain N-1231 (ATCC accession number 31565).

19. (Previously presented) The enhanced *Actinosynnema* strain according to claim 16, wherein the enhanced strain produces an ansamitocin in an amount of between 5-fold and 10-fold more than the amount produced *Actinosynnema pretiosum* strain N-1231 (ATCC accession number 31565).

20. (Previously presented) The enhanced *Actinosynnema* strain according to claim 16, wherein the ansamitocin is ansamitocin P-3.

21. (Withdrawn) A method for producing an ansamitocin, which comprises cultivating the enhanced *Actinosynnema* strain of claim 16 in a culture medium comprising a suitable carbon source.

22. (Withdrawn) The method of claim 21, wherein said ansamitocin is one or more ansamitocins of formula (I) or isomers thereof:



37. (Withdrawn) The method of claim 34, wherein the mutagen is UV light or 1-methyl-3-nitro-1-nitroso-guanidine.

38. (Previously presented) The method of claim 34, wherein the enhanced *Actinosynnema* strain produces an ansamitocin in an amount of between 1.2-fold and 10-fold more than the amount produced by the parental *Actinosynnema* strain.

39. (Previously presented) The method of claim 34, wherein the enhanced *Actinosynnema* strain produces an ansamitocin in an amount of between 1.8-fold and 10-fold more than the amount produced by the parental *Actinosynnema* strain.

40. (Previously presented) The method of claim 34, wherein the enhanced *Actinosynnema* strain produces an ansamitocin in an amount of between 5-fold and 10-fold more than the amount produced by the parental *Actinosynnema* strain.

41. (Withdrawn) The method of claim 34, wherein the selective pressure comprises growth of the treated bacteria on CM4-1 media.

42.-49. (Canceled).